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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/871,491	05/31/2001	David H. Raulet	B01-088-1	8724

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EXAMINER	
HARRIS, ALANA M	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 02/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/871,491	RAULET ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39,45,51 and 53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39, 45, 51 and 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Claims 39, 45, 51 and 53 are pending.

Claims 39 and 51 have been amended.

Claims 40-44, 46-50, 52 and 54 have been cancelled.

Claims 39, 45, 51 and 53 are examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objection

Claim Objections

3. Claims 39 and 51 are no longer objected. Claims 40-44, 46-50, 52 and 54 have been cancelled.

Withdrawn Rejections

Claim Rejections - 35 USC § 112

4. The rejection of claims 39, 45, 51 and 53 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for inhibiting prostate tumor growth and primary mammary tumor growth in a mammalian host, does not reasonably provide enablement for the said method including the administration of a NKG2D transduced cell to a mammalian host *predisposed* to having the said tumors is withdrawn in light of the claim amendments and cancellation of claims. Claims 40-44, 46-50, 52 and 54 have been cancelled.

5. The rejection of claims 39, 45, 51 and 53 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention has been withdrawn in light of the cancellation of claims 40 and 52. Claims 40-44, 46-50, 52 and 54 have been cancelled.

Maintained Rejection

Claim Rejections - 35 USC § 103

6. The rejection of claims 39, 45, 51 and 53 under 35 U.S.C. 103(a) as being unpatentable over Diefenbach et al. (Nature Immunology 1(2): 119-126, 2000), and further in view of WO 98/19167 (7 May 1998) is maintained. Claims 40-44, 46-50, 52 and 54 have been cancelled.

Applicants argue "[t]here is nothing in Diefenbach that suggests that multivalent NKG2D reagents could be used to inhibit tumor growth", nor that "...Diefenbach ...suggests or even relates to inhibition of tumor growth". Applicants continue to aver that "[t]here is nothing in WO 98/19167 that suggests that multivalent NKG2D reagents could be used to inhibit tumor growth" or the "...teaching or suggesting how MICA or MICB or MICA- or MICB-binding agents could be used in any therapy". These arguments and points of view have been carefully considered but found to be unpersuasive.

Diefenbach teaches the expression of multivalent NKG2D ligands, H-60 and Rae1β to a host compatible tumor cell, see Abstract; page 121, Figure 3b caption; page 121, bridging paragraph of columns 1 and 2. As set forth in Paper number 8 mailed

October 28, 2003 Diefenbach also teaches target cell killing, page 123, Figure 6; page 123, column 1 and first sentence of column 2. This effect in and of itself is regarded as effective inhibition of tumor growth. Furthermore, the multivalent system taught by Diefenbach is evidenced to stimulate cytotoxicity and IFN-γ by natural killer (NK) cells and TNF-α and nitric oxide production by activated macrophages. "These features suggest a general role of the NKG2D-ligand system in innate immunity", page 124, column 1, Discussion section. Diefenbach teaches that production of a tumor cell encompassing multivalent NKG2D could be done and would be efficient in an in vivo setting because of the ease and the efficiency of making the said cells, as well as the art-established fact that NKG2D ligands play a role in innate immunity.

Diefenbach is silent in teaching the methods of inhibiting prostate tumor growth or primary mammary tumor growth in a mammalian host comprising administering to the said host a composition comprising a multivalent NKG2D-binding moieties (i.e. MICA, MICB and ULBP) effective to inhibit growth of the tumor and detection of the resulting inhibition of tumor growth.

However, the WO document provides a method of increasing the expression of MHC-related molecules such as NKG2D ligands, MICA or MICB on tumor cells for a therapeutic effect in the treatment of cancer, see page 5, lines 13-25; page 6, column 4-12; page 57, lines 9-16. This is indeed contemplation of therapy. The WO document's composition comprising the NKG2D ligands as well as attached binding agents also provides the impetus for one of ordinary skill in the art to combine the two references with a reasonable expectation of success.

Moreover, WO document further provides motivation to administer tumor cells expressing NKG2D binding moieties for cancer treatment, including breast and prostate cancer, see page 4, lines 7-17. Given the WO document implements a

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to transduce other NKG2D binding moieties such as MICA, MICB or ULBP to a host-compatible cell in order to implement these cells in methods of inhibiting prostate tumor growth, as well as primary mammary tumor growth. The success of the co-expression Rae1 and H-60 onto tumor cells provides motivation to implement the teachings for multivalent expression of NKG2D binding moieties. For the reasons of record and the analysis set forth above the rejection is maintained.

Conclusion

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (703) 306-5880. The examiner can normally be reached on 7:00 am to 4:30 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne "Bonnie" Eyler, Ph.D. can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER

Alana M. Harris, Ph.D.
12 February 2004